PCT/US99/30000

```
          10         20         30         40         50         60
TTAGCGCCAT TGCCATAGAG AGACCTCAGC CATCAATCAC TAGCACATGA TTGACAGACA  60
GAGAATGGGA CTTTGGGCTT TGGCAATTCT GACACTTCCC ATGTATTTGA CAGTTACGGA 120
GGGCAGTAAA TCGTCCTGGG GTCTGGAAAA TGAGGCTTTA ATTGTGAGAT GCCCCCAAAG 180
AGGACGCTCG ACTTATCCTG TGGAATGGTA TTACTCAGAT ACAAATGAAA GTATTCCTAC 240
CCAAAAAAAA AAAAA                                                  255
```

FIG. 1

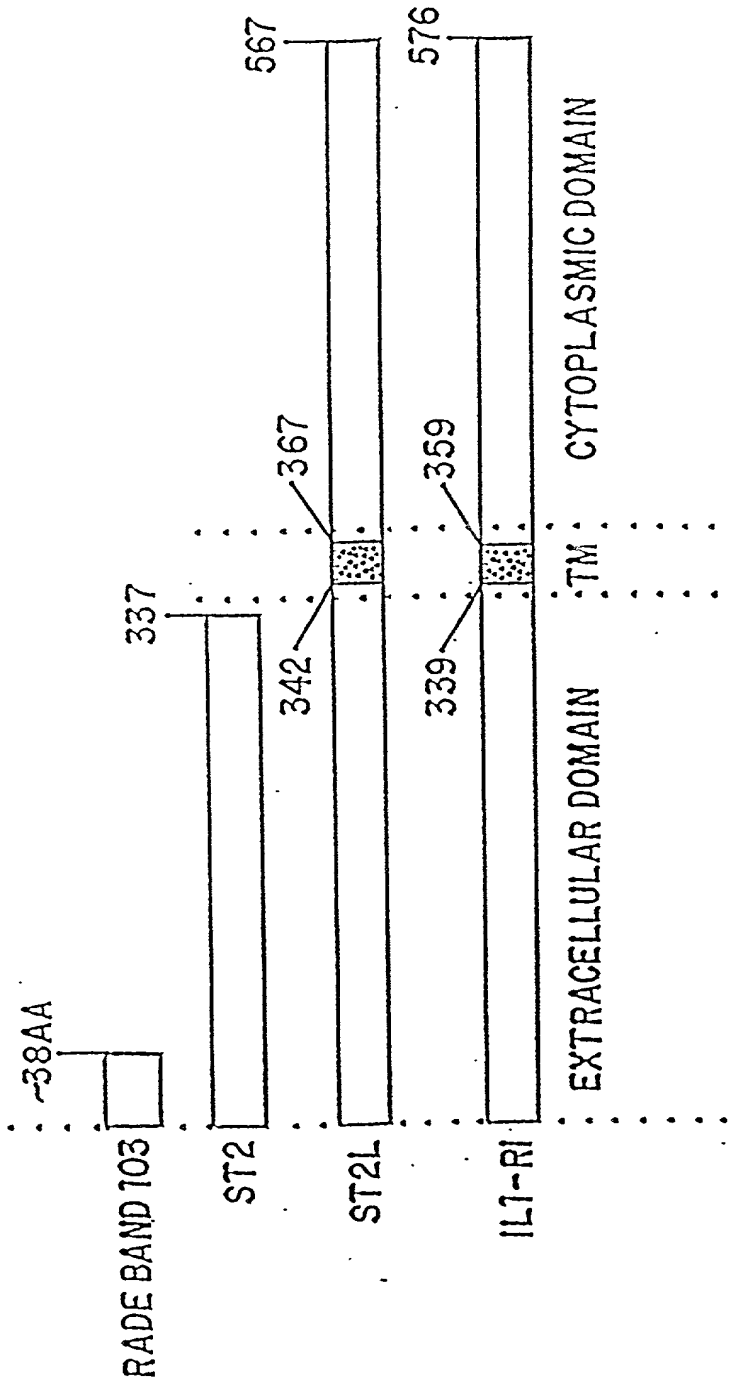
38AA
RADE BAND 103
337
ST2
342
367
ST2L
339
359
IL1-RI
567
576
TM
EXTRACELLULAR DOMAIN
CYTOPLASMIC DOMAIN

FIG. 2

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```
   1 atgattgaca gacagagaat gggactttgg gctttggcaa ttctgacact tcccatgtat
  61 ttgacagtta cggagggcag taaatcgtcc tggggtctgg aaaatgaggc tttaattgtg
 121 agatgccccc aaagaggacg ctcgacttat cctgtggaat ggtattactc agatacaaat
 181 gaaagtattc ctactcaaaa aagaaatcgg atctttgtct caagagatcg tctgaagttt
 241 ctaccagcca gagtcgaaga ctctgggatt tatgcttgtg ttatcagaag ccccaacttg
 301 aataagactg gatacttgaa tgtcaccata cataaaaagc cgccaagctg caatatccct
 361 gattatttga tgtactcgac agtacgtgga tcagataaaa atttcaagat aagctgtcca
 421 acaattgacc tgtataattg gacagcacct gttcagtggt ttaagaactg caaagctctc
 481 caagagccaa ggttcagggc acacaggtcc tacttgttca ttgacaacgt gactcatgat
 541 gatgaaggtg actacacttg tcaattcaca cacgcggaga atggaaccaa ctacatcgtg
 601 acggccacca gatcattcac agttgaagaa aaaggctttt ctatgtttcc agtaattaca
 661 aatcctccat acaaccacac aatggaagtg gaaataggaa aaccagcaag tattgcctgt
 721 tcagcttgct ttggcaaagg ctctcacttc ttggctgatg tcctgtggca gattaacaaa
 781 acagtagttg gaaattttgg tgaagcaaga attcaagaag aggaaggtcg aaatgaaagt
 841 tccagcaatg acatggattg tttaacctca gtgttaagga taactggtgt gacagaaaag
 901 gacctgtccc tggaatatga ctgtctggcc ctgaaccttc atggcatgat aaggcacacc
 961 ataaggctga gaaggaaaca accaagtaag gagtgtccct cacacattgc t
```

FIG. 3A

MIDRQRMGLWALAILTLPMYLTVTEGSKSSWGLENEALIVRCPQRGRSTYPVEWYYSD
TNESIPTQKRNRIFVSRDRLKFLPARVEDSGIYACVIRSPNLNKTGYLNVTIHKKPPSCNIP
DYLMYSTVRGSDKNFKITCPTIDLYNWTAPVQWFKNCKALQEPRFRAHRSYLFIDNVTH
DDEGDYTCQFTHAENGTNYIVTATRSFTVEEKGFSMFPVITNPPYNHTMEVEIGKPASIA
CSACFGKGSHFLADVLWQINKTVVGNFGEARIQEEEGRNESSSNDMDCLTSVLRITGVT
EKDLSLEYDCLALNLHGMIRHTIRLRRKQPSKECPSHIA

FIG. 3B

```
   1 tgccattgcc atagagagac ctcagccatc aatcactagc acatgattga cagacagaga
  61 atgggacttt gggctttggc aattctgaca cttcccatgt atttgacagt tacggagggc
 121 agtaaatcgt cctggggtct ggaaaatgag gctttaattg tgagatgccc ccaaagagga
 181 cgctcgactt atcctgtgga atggtattac tcagatacaa atgaaagtat tcctactcaa
 241 aaaagaaatc ggatctttgt ctcaagagat cgtctgaagt ttctaccagc cagagtggaa
 301 gactctggga tttatgcttg tgttatcaga agccccaact tgaataagac tggatacttg
 361 aatgtcacca tacataaaaa gccgccaagc tgcaatatcc ctgattattt gatgtactcg
 421 acagtacgtg gatcagataa aaatttcaag ataacgtgtc caacaattga cctgtataat
 481 tggacagcac ctgttcagtg gtttaagaac tgcaaagctc tccaagagcc aaggttcagg
 541 gcacacaggt cctacttgtt cattgacaac gtgactcatg atgatgaagg tgactacact
 601 tgtcaattca cacacgcgga gaatggaacc aactacatcg tgacggccac cagatcattc
 661 acagttgaag aaaaaggctt ttctatgttt ccagtaatta caaatcctcc atacaaccac
 721 acaatggaag tggaaatagg aaaaccagca agtattgcct gttcagcttg ctttggcaaa
 781 ggctctcact tcttggctga tgtcctgtgg cagattaaca aaacagtagt tggaaatttt
 841 ggtgaagcaa gaattcaaga agaggaaggt cgaaatgaaa gttccagcaa tgacatggat
 901 tgtttaacct cagtgttaag gataactggt gtgacagaaa aggacctgtc cctggaatat
 961 gactgtctgg ccctgaacct tcatggcatg ataaggcaca ccataaggct gagaaggaaa
1021 caaccaattg atcaccgaag catctactac atagttgctg gatgtagttt attgctaatg
1081 tttatcaatg tcttggtgat agtcttaaaa gtgttctgga ttgaggttgc tctgttctgg
1141 agagatatag tgacacctta caaaacccgg aacgatggca agctctacga tgcgtacatc
1201 atttaccctc gggtcttccg gggcagcgcg gcgggaaccc actctgtgga gtactttgtt
1261 caccacactc tgcccgacgt tcttgaaaat aaatgtggct acaaattgtg catttatggg
1321 agagacctgt tacctgggca agatgcagcc accgtggtgg aaagcagtat ccagaatagc
1381 agaagacagg tgtttgttct ggcccctcac atgatgcaca gcaaggaatt tgcctacgag
1441 caggagattg ctctgcacag cgccctcatc cagaacaact ccaaggtgat tcttattgaa
1501 atggagcctc tgggtgaggc aagccgacta caggttgggg acctgcaaga ttctctccag
1561 catcttgtga aaattcaggg gaccatcaag tggagggaag atcatgtggc cgacaagcag
1621 tctctaagtt ccaaattctg gaagcatgtg aggtaccaaa tgccagtgcc agaaagagcc
1681 tccaagacgg catctgttgc ggctccgttg agtggcaagg catgcttaga cctgaaacac
1741 ttttgagttg agagctgcgg agtcccagca gtaggcaccg gagtgcaggt gtgcagactt
1801 gaaatgccaa gggtgggggc cccaagtctc agctaaagag caactctagt ttatttcct
1861 ggttatggta ggagccaccc atcgtttgtt tccggtttcc ttttcctact tcactcttgt
1921 ggcacaagat caaccctgag ctttttcctt ttcttttatt tctcttttg ttccttcttt
1981 taaaagcttt ttaaaattga ttatcttatt tatctacctt tcaaaggtta tccccttcc
2041 cggtgccccc tctacaaatc cccatcctgc ttccctcctc cctgcttcta tgagggtgcc
2101 cccccacctg cccatccact ccagccttac aggccttgtg ttcccctatg ctggggcatc
2161 gagcctccat aagacctccc ctctcattca tcaattatct acattctgaa tatcaagccg
2221 acacttttgt ttttgttttt gatttttga gacagggttt ctctgtgtag ccctggctgt
2281 cttgaaactc acattgtaga ccaggctggc ctcgaactca gaaatcagcc tgcctctgcc
2341 tccccgagtg ctgggattaa aggcgtgcgc caccacgccg ggctaagcct acactttcag
2401 aataaagttc tgattcacct caaagagcag tctcattccc agaggcagag agccggaaag
2461 agcctccaat gtgcttgtcc aggcagagct gaccttattt gcttaccagt cacaggtaaa
2521 caaagcgttt ctccgtgttg cctcttgtag acatccctgt aatagattag gaagggaatg
2581 agccgtccta ctgaccagtt tgtgaattgt ggtagaaaaa gcgttgacgt ttgttaaata
2641 cttgttagca atgtaaacct cattcctaac acaccagaat ttcttacttt ttattcgtca
2701 attaccgagt tttgtcaagt cagtattaac agatttggtc gaatacctta cccaaattgc
2761 cattacagtc gagcatgttt tcagttctaa atgcctttta tatatttttt attcttctta
2821 gaaatacttc ctcactttaa aagtaatgta aagatgtgtt agaaaacata aggtgtaaga
2881 gaaagtatga taaaatataa aaaataatag aaaggaaagg aaatataatg aaaatcataa
2941 ctcttaagat taattttggt aggtctgtat tttaaaatat aattaaattt tataccgata
3001 acttttatag ctgagattgt acactacaga ctaggcagct tttcctattt accaccataa
3061 tgaaaactgg tggctgattt ctttaacatt cacagaagtt ccaaatgtct cattttagac
3121 tgtgctgcag actatggctg aagcagccag aatgagaaac aggtctgcca tgtcacatcg
3181 ggacattttc ctacttactg aaatgtatct gtcactgtgc gacagctaac ttttgtgata
3241 ctcctatgaa atgtgtaggg aatttggaca gaacagaatc aatctatagt cagaggtcct
3301 ctggacagtc ttttccagga gcacacacag accgtgaggt cctaggcacc caggaaacgg
3361 atccagagcc caggcaagtg tcttacaggt accttgaatt ttgccaatag atatgagccc
3421 tgccttagct gagttgctca gtcggtgatg ggactccagg ctgaggtgac aatgaacaca
```

FIG. 4A

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```
3481 gaatttggga gactcttgaa aggaggggaa tgttgaactc acggtcaaca tatgaggctg
3541 cagagaagcc gtatgcagaa gtgtgtgtag aggatctaga gtagcccgtt tctctgggga
3601 cagtgtgctc ttagtctgta cccttaggct gggttgccag gtaaacattt gctagtgttc
3661 agttcaaagg ctgaagcttg agctgagggt gatgaggaat tcaaacttcc cctcgcatgc
3721 atccaccctg tggttgcctg gtttgctaag tccacctgct ctgctgtagt agaaggtttt
3781 gatcttctgc agcttcatct acttcttagt gagttgccaa aactgaccac tgaaaagcat
3841 gctgtgtaca taactgtctc atgtcccaga acgtgcaatc aggaggaagt cctcactccc
3901 gataacggaa tccttgctct gtggctgtga ggacgtccct tagcaacctc agatagtaat
3961 ttttcttagg ttggatggaa catagtaacg tgctggattc tttgctaact gaaaatagaa
4021 gtattcggat ttcagaaaga actggataaa tattaatgtt ggtgattatg aaatctcatt
4081 gtgagccgtg tgagtttgag tgtgtattcc atgattgtgc tgaatgaaga cctctaaaaa
4141 tgaaattctc tccaatctca tccctgggaa tagttgcttc ctcatgcctg ctgctccatc
4201 catggaaaat gactaaagag aattattatt tgttcccgag attcttctga taagtctaaa
4261 ctatttgcat gtaattgagc tgggcagcat ggcacacttg ggaggcagag gcaggtggat
4321 ctctgtgagt ttgaggccag cctgctctac agagttagtt ccaggacacc agagctacaa
4381 aaagaaaacc tgtcctaaca acaacagcaa cagctgcagc agcaacaaca acaacaaaga
4441 aaaagaagag gaggaggagg aaaggaaaga aggaagaagg aagaagaaag ggaagaaata
4501 atagattttt ctgtaatgaa cacacatatg ctttgatgct tttgctaaac tcaaaatatt
4561 agttttattt tactgttttg aaaggttcaa agcatgatcc atgtaaaaat gtcttctgtg
4621 gggctttctc ccatttctac ttttgttccc ctcatttctt caaagtgctt gtccaggcag
4681 agctgacctt atttgcttac cagttacagg taaacaaagc gtttcctcgt gttgcctctt
4741 gtagccatct ctgtattaga ttaggaaggg aaggagccgt cctactgtcc agtttgtgag
4801 ttctggtaga aagagtgttg aagtttgtta aatgcttgtt ttccatgtat caaaatgtta
4861 tgcctttcct atttattatt gtatgacaaa ttatttttca ctgggcaaaa ataattgtgc
4921 cattgactcc ttgtgtgttt tcttcatgtg tgtttgaaga gttctagctt attaaaaaaa
4981 aaaatctag
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FIG. 4A CONTD

MIDRQRMGLWALAILTLPMYLTVTEGSKSSWGLENEALIVRCPQRGRSTYPVEWYYSD
TNESIPTQKRNRIFVSRDRLKFLPARVEDSGIYACVIRSPNLNKTGYLNVTIHKKPPSCNIP
DYLMYSTVRGSDKNFKITCPTIDLYNWTAPVQWFKNCKALQEPRFRAHRSYLFIDNVTH
DDEGDYTCQFTHAENGTNYIVTATRSFTVEEKGFSMFPVITNPPYNHTMEVEIGKPASIA
CSACFGKGSHFLADVLWQINKTVVGNFGEARIQEEEGRNESSSNDMDCLTSVLRITGVT
EKDLSLEYDCLALNLHGMIRHTIRLRRKQPIDHRSIYYIVAGCSLLLMFINVLVIVLKVFW
IEVALFWRDIVTPYKTRNDGKLYDAYIIYPRVFRGSAAGTHSVEYFVHHTLPDVLENKC
GYKLCIYGRDLLPGQDAATVVESSIQNSRRQVFVLAPHMMHSKEFAYEQEIALHSALIQ
NNSKVILIEMEPLGEASRLQVGDLQDSLQHLVKIQGTIKWREDHVADKQSLSSKFWKHV
RYQMPVPERASKTASVAAPLSGKACLDLKHF

FIG. 4B

```
   1 aaagagaggc tggctgttgt atttagtaaa gctataaagc tgtaagagaa attggctttc
  61 tgagttgtga aactgtgggc agaaagttga ggaagaaaga actcaagtac aacccaatga
 121 ggttgagata taggctactc ttcccaactc agtcttgaag agtatcacca actgcctcat
 181 gtgtggtgac cttcactgtc gtatgccagt gactcatctg gagtaatctc aacaacgagt
 241 taccaatact tgctcttgat tgataaacag aatggggttt tggatcttag caattctcac
 301 aattctcatg tattccacag cagcaaagtt tagtaaacaa tcatggggcc tggaaaatga
 361 ggctttaatt gtaagatgtc ctagacaagg aaaacctagt tacaccgtgg attggtatta
 421 ctcacaaaca aacaaaagta ttcccactca ggaaagaaat cgtgtgtttg cctcaggcca
 481 acttctgaag tttctaccag ctgaagttgc tgattctggt atttatacct gtattgtcag
 541 aagtcccaca ttcaatagga ctggatatgc gaatgtcacc atatataaaa aacaatcaga
 601 ttgcaatgtt ccagattatt tgatgtattc aacagtatct ggatcagaaa aaaattccaa
 661 aatttattgt cctaccattg acctctacaa ctggacagca cctcttgagt ggtttaagaa
 721 ttgtcaggct cttcaaggat caaggtacag ggcgcacaag tcatttttgg tcattgataa
 781 tgtgatgact gaggacgcag gtgattacac ctgtaaattt atacacaatg aaaatggagc
 841 caattatagt gtgacggcga ccaggtcctt cacggtcaag gatgagcaag gcttttctct
 901 gtttccagta atcggagccc ctgcacaaaa tgaaataaag gaagtggaaa ttggaaaaaa
 961 cgcaaaccta acttgctctg cttgttttgg aaaaggcact cagttcttgg ctgccgtcct
1021 gtggcagctt aatggaacaa aaattacaga ctttggtgaa ccaagaattc aacaagagga
1081 agggcaaaat caaagtttca gcaatgggct ggcttgtcta gacatggttt taagaatagc
1141 tgacgtgaag gaagaggatt tattgctgca gtacgactgt ctggccctga atttgcatgg
1201 cttgagaagg cacaccgtaa gactaagtag gaaaaatcca attgatcatc atagcatcta
1261 ctgcataatt gcagtatgta gtgtattttt aatgctaatc aatgtcctgg ttatcatcct
1321 aaaaatgttc tggattgagg ccactctgct ctggagagac atagctaaac cttacaagac
1381 taggaatgat ggaaagctct atgatgctta tgttgtctac ccacggaact acaaatccag
1441 tacagatggg gccagtcgtg tagagcactt tgttcaccag attctgcctg atgttcttga
1501 aaataaatgt ggctatacct tatgcattta tgggagagat atgctacctg gagaagatgt
1561 agtcactgca gtggaaacca acatacgaaa gagcaggcgg cacattttca tcctgacccc
1621 tcagatcact cacaataagg agtttgccta cgagcaggag gttgccctgc actgtgccct
1681 catccagaac gacgccaagg tgatacttat tgagatggag gctctgagcg agctggacat
1741 gctgcaggct gaggcgcttc aggactccct ccagcatctt atgaaagtac aggggaccat
1801 caagtggagg gaggaccaca ttgccaataa aaggtccctg aattccaaat tctggaagca
1861 cgtgaggtac caaatgcctg tgccaagcaa aattcccaga aaggcctcta gtttgactcc
1921 cttggctgcc cagaagcaat agtgcctgct gtgatgtgca aagggatctg ggtttgaagc
1981 tttcctgact tctcctagct ggcttatgcc cctgcactga agtgtgagga gcgggaatat
2041 taaagggatt caggccac
```

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FIG. 5A

```
  1 mgfwilailt ilmystaakf skqswglene alivrcprqg kpsytvdwyy sqtnksiptq
 61 ernrvfasgq llkflpaeva dsgiytcivr sptfnrtgya nvtiykkqsd cnvpdylmys
121 tvsgseknsk iycptidlyn wtaplewfkn cqalqgsryr ahksflvidn vmtedagdyt
181 ckfihnenga nysvtatrsf tvkdeqgfsl fpvigapaqn eikeveigkn anltcsacfg
241 kgtqflaavl wqlngtkitd fgepriqqee gqnqsfsngl acldmvlria dvkeedlllq
301 ydclalnlhg lrrhtvrlsr knpidhhsiy ciiavcsvfl mlinvlviil kmfwieatll
361 wrdiakpykt rndgklyday vvyprnykss tdgasrvehf vhqilpdvle nkcgytlciy
421 grdmlpgedv vtavetnirk srrhifiltp qithnkefay eqevalhcal iqndakvili
481 emealseldm lqaealqdsl qhlmkvqgti kwredhiank rslnskfwkh vryqmpvpsk
541 iprkassltp laaqkq
```

FIG. 5B

```
   1 atctcaacaa cgagttacca atacttgctc ttgattgata aacagaatgg ggttttggat
  61 cttagcaatt ctcacaattc tcatgtattc cacagcagca aagtttagta aacaatcatg
 121 gggcctggaa aatgaggctt taattgtaag atgtcctaga caaggaaaac ctagttacac
 181 cgtggattgg tattactcac aaacaaacaa aagtattccc actcaggaaa gaaatcgtgt
 241 gtttgcctca ggccaacttc tgaagtttct accagctgaa gttgctgatt ctggtattta
 301 tacctgtatt gtcagaagtc ccacattcaa taggactgga tatgcgaatg tcaccatata
 361 taaaaaacaa tcagattgca atgttccaga ttatttgatg tattcaacag tatctggatc
 421 agaaaaaaat tccaaaattt attgtcctac cattgacctc tacaactgga cagcacctct
 481 tgagtggttt aagaattgtc aggctcttca aggatcaagg tacagggcgc acaagtcatt
 541 tttggtcatt gataatgtga tgactgagga cgcaggtgat tacacctgta aatttataca
 601 caatgaaaat ggagccaatt atagtgtgac ggcgaccagg tccttcacgg tcaaggatga
 661 gcaaggcttt tctctgtttc cagtaatcgg agcccctgca caaaatgaaa taaaggaagt
 721 ggaaattgga aaaaacgcaa acctaacttg ctctgcttgt tttggaaaag gcactcagtt
 781 cttggctgcc gtcctgtggc agcttaatgg aacaaaaatt acagactttg gtgaaccaag
 841 aattcaacaa gaggaagggc aaaatcaaag tttcagcaat gggctggctt gtctagacat
 901 ggttttaaga atagctgacg tgaaggaaga ggatttattg ctgcagtacg actgtctggc
 961 cctgaatttg catggcttga gaaggcacac cgtaagacta agtaggaaaa atccaagtaa
1021 ggagtgtttc tgagactttg atcacctgaa ctttctctag caagtgtaag cagaatggag
1081 tgtggttcca agagatccat caagacaatg ggaatggcct gtgccataaa atgtgcttct
1141 cttcttcggg atgttgtttg ctgtctgatc tttgtagact gttcctgttt gctgggagct
1201 tctctgctgc ttaaattgtt cgtcctcccc cactccctcc tatcgttggt ttgtctagaa
1261 cactcagctg cttctttggt catccttgtt ttctaacttt atgaactccc tctgtgtcac
1321 tgtatgtgaa aggaaatgca ccaacaaccg aaaactg
```

FIG. 6A

MGFWILAILTILMYSTAAKFSKQSWGLENEALIVRCPRQGKPSYTVDW
YYSQTNKSIPTQERNRVFASGQLLKFLPAEVADSGIYTCIVRSPTFNRT
GYANVTIYKKQSDCNVPDYLMYSTVSGSEKNSKIYCPTIDLYNWTAPL
EWFKNCQALQGSRYRAHKSFLVIDNVMTEDAGDYTCKFIHNENGAN
YSVTATRSFTVKDEQGFSLFPVIGAPAQNEIKEVEIGKNANLTCSACFG
KGTQFLAAVLWQLNGTKITDFGEPRIQQEEGQNQSFSNGLACLDMVL
RIADVKEEDLLLQYDCLALNLHGLRRHTVRLSRKNPSKECF

FIG. 6B

Express Mail No. EV 339 909 945 US

```
   1 cttagctccg tcactgactc caagttcatc ccctctgtct ttcagtttgg ttgagatata
  61 ggctactctt cccaactcag tcttgaagag tatcaccaac tgcctcatgt gtggtgacct
 121 tcactgttgt atgccagtga ctcatctgga gtaatctcaa caacgagtta ccaatacttg
 181 ctcttgattg ataaacagaa tggggttttg gatcttagca attctcacaa ttctcatgta
 241 ttccacagca gcaaagttta gtaaacaatc atggggcctg gaaaatgagg ctttaattgt
 301 aagatgtcct agacaaggaa aacctagtta caccgtggat tggtattact cacaaacaaa
 361 caaaagtatt cccactcagg aaagaaatcg tgtgtttgcc tcaggccgac ttctgaagtt
 421 tctaccagct gaagttgctg attctggtat ttatacctgt attgtcagaa gtcccacatt
 481 caataggact ggatatgcga atgtcaccat atataaaaaa caatcagatt gcaatgttcc
 541 agattatttg atgtattcaa cagtatctgg atcagaaaaa aattccaaaa tttattgtcc
 601 taccattgac ctctacaact ggacagcacc tcttgagtgg tttaagaatt gtcaggctct
 661 tcaaggatca aggtacaggg cgcacaagtc atttttggtc attgataatg tgatgactga
 721 ggacgcaggt gattacacct gtaaatttat acacaatgaa aatggagcca attatagtgt
 781 gacggcgacc aggtccttca cggtcaaggt ttggtgtcag agtttctgca aattaaaaaa
 841 gagcttaatc tttagtaata ctcattggat tcaaagtcta atgagaggct ttgtgatggt
 901 atactatggt gtacataaat gttgtcgagt ggtttttaat ctttgtttgc aatactttca
 961 acatcatcaa tggccttgaa tgagcaaggc ttttctctgt ttccagtaat cggagcccct
1021 gcacaaaatg aaataaagga agtggaaatt ggaaaaaacg caaacctaac ttgctctgct
1081 tgttttggaa aaggcactca gttcttggct gccgtcctgt ggcagcttaa tggaacaaaa
1141 attacagact ttggtgaacc aagaattcaa caagaggaag ggcaaaatca aagtttcagc
1201 aatgggctgg cttgtctaga catggtttta agaatagctg acgtgaagga agaggattta
1261 ttgctgcagt acgactgtct ggccctgaat ttgcatggct tgagaaggca caccgtaaga
1321 ctaagtagga aaaatccaag taaggagtgt ttctgagact ttgatcacct gaactttctc
1381 tagcaagtgt aagcagaatg gagtgtggtt ccaagagatc catcaagaca atgggaatgg
1441 cctgtgccat aaaatgtgct tctcttcttc gggatgttgt ttgctgtctg atctttgtag
1501 actgttcctg tttgctggga gcttctctgc tgcttaaatt gttcgtcctc ccccactccc
1561 tcctatcgtt ggtttgtcta gaacactcag ctgcttcttt ggtcatcctt gttttctaac
1621 tttatgaact ccctctgtgt cactgtatgt gaaaggaaat gcaccaacaa ccgaaaactg
```

FIG. 7A

```
  1 mgfwilailt ilmystaakf skqswglene alivrcprqg kpsytvdwyy sqtnksiptq
 61 ernrvfasgr llkflpaeva dsgiytcivr sptfnrtgya nvtiykkqsd cnvpdylmys
121 tvsgseknsk iycptidlyn wtaplewfkn cqalqgsryr ahksflvidn vmtedagdyt
181 ckfihnenga nysvtatrsf tvkvwcqsfc klkkslifsn thwiqslmrg fvmvyygvhk
241 ccrvvfnlcl qyfqhhqwp
```

FIG. 7B

D20030190014

```
GTCGACCCACGCGTCCGCCCACGCGTCCGCTGGAGTAATCTCAACAACGAGTTACCAATACTTGCTCTTGATTGATAAA  79

      M   G   F   W   I   L   A   I   L   T   I   L   M   Y   S   T   A   A      18
CAGA ATG GGG TTT TGG ATC TTA GCA ATT CTC ACA ATT CTC ATG TAT TCC ACA GCA GCA      137

 K   F   S   K   Q   S   W   G   L   E   N   E   A   L   I   V   R   C   P   R   38
AAG TTT AGT AAA CAA TCA TGG GGC CTG GAA AAT GAG GCT TTA ATT GTA AGA TGT CCT AGA  197

 Q   G   K   P   S   Y   T   V   D   W   Y   Y   S   Q   T   N   K   S   I   P   58
CAA GGA AAA CCT AGT TAC ACC GTG GAT TGG TAT TAC TCA CAA ACA AAC AAA AGT ATT CCC  257

 T   Q   E   R   N   R   V   F   A   S   G   Q   L   L   K   F   L   P   A   A   78
ACT CAG GAA AGA AAT CGT GTG TTT GCC TCA GGC CAA CTT CTG AAG TTT CTA CCA GCT GCA  317

 V   A   D   S   G   I   Y   T   C   I   V   R   S   P   T   F   N   R   T   G   98
GTT GCT GAT TCT GGT ATT TAT ACC TGT ATT GTC AGA AGT CCC ACA TTC AAT AGG ACT GGA  377

 Y   A   N   V   T   I   Y   K   K   Q   S   D   C   N   V   P   D   Y   L   M   118
TAT GCG AAT GTC ACC ATA TAT AAA AAA CAA TCA GAT TGC AAT GTT CCA GAT TAT TTG ATG  437

 Y   S   T   V   S   G   S   E   K   N   S   K   I   Y   C   P   T   I   D   L   138
TAT TCA ACA GTA TCT GGA TCA GAA AAA AAT TCC AAA ATT TAT TGT CCT ACC ATT GAC CTC  497

 Y   N   W   T   A   P   L   E   W   F   K   M   S   K   A   F   L   C   F   Q   158
TAC AAC TGG ACA GCA CCT CTT GAG TGG TTT AAG ATG AGC AAG GCT TTT CTC TGT TTC CAG  557

*                                                                                159
TAA                                                                              560

TCGGAGCCCCTGCACAAAATGAAATAAAGGAAGTGGAAATTGGCACTCAGTTCTTGGCTGCCGTCCTGTGGCAGCTTAA  639

TGGAACAAAAATTACAGACTTTGGTGAACCAAGAATTCAACAAGAGGAAGGGCAAAATCAAAGTTTCAGCAATGGGCTG  718

GCTTGTCTAGACATGGTTTTAAGAATAGCTGACGTGAAGGAAGAGGATTTATTGCTGCAGTACGACTGTCTGGCCCTGA  797

ATTTGCATGGCTTGAGAAGGCACACCGTAAGACTAAGTAGGAAAAATCCAAGTAAGGAGTGTTTCTGAGACTTTGATCA  876

CCTGAACTTTCTCTAGCAAGTGTAAGCAGAATGGAGTGTGGTTCCAAGAGATCCATCAAGACAATGGGAATGGCCTGTG  955

CCATAAAATGTGCTTCTCTTCTTCGGGATGTTGTTTGCTGTCTGATCTTTGTAGACTGTTCCTGTTTGCTGGGAGCTTC 1034

TCTGCTGCTTAAATTGTTCGTCCTCCCCCACTCCCTCCTATCGTTGGTTTGTCTAGAACACTCAGCTGCTTCTTTGGTC 1113

ATCCTTGTTTTCTAACTTTATGAACTCCCTCTGTGTCACTGTATGTGAAAGGAAATGCACCAACAACCGTAAAAAAAAA 1192

AAAAAAAGGGCGGCCGCT                                                               1210
```

09/09/2003 - 03:25:01

FIG. 8

```
P14719          MIDRQRMGLW ALAILTLPMY LTVTEGSKSS WGLENEALIV RCPQRGRSTY
S29498          MIDRQRMGLW ALAILTLPMY LTVTEGSKSS WGLENEALIV RCPQRGRSTY

P14719          PVEWYYSDTN ESIPTQKRNR IFVSRDRLKF LPARVEDSGI YACVIRSPNL
S29498          PVEWYYSDTN ESIPTQKRNR IFVSRDRLKF LPARVEDSGI YACVIRSPNL

P14719          NKTGYLNVTI HKKPPSCNIP DYLMYSTVRG SDKNFKITCP TIDLYNWTAP
S29498          NKTGYLNVTI HKKPPSCNIP DYLMYSTVRG SDKNFKITCP TIDLYNWTAP

P14719          VQWFKNCKAL QEPRFRAHRS YLFIDNVTHD DEGDYTCQFT HAENGTNYIV
S29498          VQWFKNCKAL QEPRFRAHRS YLFIDNVTHD DEGDYTCQFT HAENGTNYIV

P14719          TATRSFTVEE KGFSMFPVIT NPPYNHTMEV EIGKPASIAC SACFGKGSHF
S29498          TATRSFTVEE KGFSMFPVIT NPPYNHTMEV EIGKPASIAC SACFGKGSHF

P14719          LADVLWQINK TVVGNFGEAR IQEEEGRNES SSNDMDCLTS VLRITGVTEK
S29498          LADVLWQINK TVVGNFGEAR IQEEEGRNES SSNDMDCLTS VLRITGVTEK

P14719          DLSLEYDCLA LNLHGMIRHT IRLRRKQPSK ECPSHIA... ..........
S29498          DLSLEYDCLA LNLHGMIRHT IRLRRKQPID HRSIYYIVAG CSLLLMFINV

P14719          .......... .......... .......... .......... ..........
S29498          LVIVLKVFWI EVALFWRDIV TPYKTRNDGK LYDAYIIYPR VFRGSAAGTH

P14719          .......... .......... .......... .......... ..........
S29498          SVEYFVHHTL PDVLENKCGY KLCIYGRDLL PGQDAATVVE SSIQNSRRQV

P14719          .......... .......... .......... .......... ..........
S29498          FVLAPHMMHS KEFAYEQEIA LHSALIQNNS KVILIEMEPL GEASRLQVGD

P14719          .......... .......... .......... .......... ..........
S29498          LQDSLQHLVK IQGTIKWRED HVADKQSLSS KFWKHVRYQM PVPERASKTA

P14719          .......... .......
S29498          SVAAPLSGKA CLDLKHF
```

FIG. 9

```
BAA82405        MGFWILAILT ILMYSTAAKF SKQSWGLENE ALIVRCPRQG KPSYTVDWYY
BAA02233        MGFWILAILT ILMYSTAAKF SKQSWGLENE ALIVRCPRQG KPSYTVDWYY
Athdc120c9      MGFWILAILT ILMYSTAAKF SKQSWGLENE ALIVRCPRQG KPSYTVDWYY
BAA85894        MGFWILAILT ILMYSTAAKF SKQSWGLENE ALIVRCPRQG KPSYTVDWYY

BAA82405        SQTNKSIPTQ ERNRVFASGQ LLKFLPAEVA DSGIYTCIVR SPTFNRTGYA
BAA02233        SQTNKSIPTQ ERNRVFASGQ LLKFLPAEVA DSGIYTCIVR SPTFNRTGYA
Athdc120c9      SQTNKSIPTQ ERNRVFASGQ LLKFLPAAVA DSGIYTCIVR SPTFNRTGYA
BAA85894        SQTNKSIPTQ ERNRVFASGR LLKFLPAEVA DSGIYTCIVR SPTFNRTGYA

BAA82405        NVTIYKKQSD CNVPDYLMYS TVSGSEKNSK IYCPTIDLYN WTAPLEWFKN
BAA02233        NVTIYKKQSD CNVPDYLMYS TVSGSEKNSK IYCPTIDLYN WTAPLEWFKN
Athdc120c9      NVTIYKKQSD CNVPDYLMYS TVSGSEKNSK IYCPTIDLYN WTAPLEWFKM
BAA85894        NVTIYKKQSD CNVPDYLMYS TVSGSEKNSK IYCPTIDLYN WTAPLEWFKN

BAA82405        CQALQGSRYR AHKSFLVIDN VMTEDAGDYT CKFIHNENGA NYSVTATRSF
BAA02233        CQALQGSRYR AHKSFLVIDN VMTEDAGDYT CKFIHNENGA NYSVTATRSF
Athdc120c9      SKAFLCFQ.. .......... .......... .......... ..........
BAA85894        CQALQGSRYR AHKSFLVIDN VMTEDAGDYT CKFIHNENGA NYSVTATRSF

BAA82405        TVK....... DEQGFSLFPV IGAPAQNEIK EVEIGKNANL TCSACFGKGT
BAA02233        TVK....... DEQGFSLFPV IGAPAQNEIK EVEIGKNANL TCSACFGKGT
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        TVKVWCQSFC KLKKSLIFSN THWIQSLMRG FVMVYYGVHK CCRVVFNLCL

BAA82405        QFLAAVLWQL NGTKITDFGE PRIQQEEGQN QSFSNGLACL DMVLRIADVK
BAA02233        QFLAAVLWQL NGTKITDFGE PRIQQEEGQN QSFSNGLACL DMVLRIADVK
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        QYFQHHQWP. .......... .......... .......... ..........

BAA82405        EEDLLLQYDC LALNLHGLRR HTVRLSRKNP IDHHSIYCII AVCSVFLMLI
BAA02233        EEDLLLQYDC LALNLHGLRR HTVRLSRKNP SKECF..... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

BAA82405        NVLVIILKMF WIEATLLWRD IAKPYKTRND GKLYDAYVVY PRNYKSSTDG
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

BAA82405        ASRVEHFVHQ ILPDVLENKC GYTLCIYGRD MLPGEDVVTA VETNIRKSRR
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

BAA82405        HIFILTPQIT HNKEFAYEQE VALHCALIQN DAKVILIEME ALSELDMLQA
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

BAA82405        EALQDSLQHL MKVQGTIKWR EDHIANKRSL NSKFWKHVRY QMPVPSKIPR
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

BAA82405        KASSLTPLAA QKQ
BAA02233        .......... ...
Athdc120c9      .......... ...
BAA85894        .......... ...
```

FIG. 10

```
P14719          MIDRQRMGLW ALAILTLPMY LTVTEGSKSS WGLENEALIV RCPQRGRSTY
S29498          MIDRQRMGLW ALAILTLPMY LTVTEGSKSS WGLENEALIV RCPQRGRSTY
BAA82405        ......MGFW ILAILTILMY STAAKFSKQS WGLENEALIV RCPRQGKPSY
BAA02233        ......MGFW ILAILTILMY STAAKFSKQS WGLENEALIV RCPRQGKPSY
Athdc120c9      ......MGFW ILAILTILMY STAAKFSKQS WGLENEALIV RCPRQGKPSY
BAA85894        ......MGFW ILAILTILMY STAAKFSKQS WGLENEALIV RCPRQGKPSY

P14719          PVEWYYSDTN ESIPTQKRNR IFVSRDRLKF LPARVEDSGI YACVIRSPNL
S29498          PVEWYYSDTN ESIPTQKRNR IFVSRDRLKF LPARVEDSGI YACVIRSPNL
BAA82405        TVDWYYSQTN KSIPTQERNR VFASGQLLKF LPAEVADSGI YTCIVRSPTF
BAA02233        TVDWYYSQTN KSIPTQERNR VFASGQLLKF LPAEVADSGI YTCIVRSPTF
Athdc120c9      TVDWYYSQTN KSIPTQERNR VFASGQLLKF LPAAVADSGI YTCIVRSPTF
BAA85894        TVDWYYSQTN KSIPTQERNR VFASGRLLKF LPAEVADSGI YTCIVRSPTF

P14719          NKTGYLNVTI HKKPPSCNIP DYLMYSTVRG SDKNFKITCP TIDLYNWTAP
S29498          NKTGYLNVTI HKKPPSCNIP DYLMYSTVRG SDKNFKITCP TIDLYNWTAP
BAA82405        NRTGYANVTI YKKQSDCNVP DYLMYSTVSG SEKNSKIYCP TIDLYNWTAP
BAA02233        NRTGYANVTI YKKQSDCNVP DYLMYSTVSG SEKNSKIYCP TIDLYNWTAP
Athdc120c9      NRTGYANVTI YKKQSDCNVP DYLMYSTVSG SEKNSKIYCP TIDLYNWTAP
BAA85894        NRTGYANVTI YKKQSDCNVP DYLMYSTVSG SEKNSKIYCP TIDLYNWTAP

P14719          VQWFKNCKAL QEPRFRAHRS YLFIDNVTHD DEGDYTCQFT HAENGTNYIV
S29498          VQWFKNCKAL QEPRFRAHRS YLFIDNVTHD DEGDYTCQFT HAENGTNYIV
BAA82405        LEWFKNCQAL QGSRYRAHKS FLVIDNVMTE DAGDYTCKFI HNENGANYSV
BAA02233        LEWFKNCQAL QGSRYRAHKS FLVIDNVMTE DAGDYTCKFI HNENGANYSV
Athdc120c9      LEWFKMSKAF LCFQ..... .......... .......... ..........
BAA85894        LEWFKNCQAL QGSRYRAHKS FLVIDNVMTE DAGDYTCKFI HNENGANYSV

P14719          TATRSFTVE. .......EKG FSMFPVITNP PYNHTMEVEI GKPASIACSA
S29498          TATRSFTVE. .......EKG FSMFPVITNP PYNHTMEVEI GKPASIACSA
BAA82405        TATRSFTVK. ......DEQG FSLFPVIGAP AQNEIKEVEI GKNANLTCSA
BAA02233        TATRSFTVK. ......DEQG FSLFPVIGAP AQNEIKEVEI GKNANLTCSA
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        TATRSFTVKV WCQSFCKLKK SLIFSNTHWI QSLMRGFVMV YYGVHKCCRV

P14719          CFGKGSHFLA DVLWQINKTV VGNFGEARIQ EEEGRNESSS NDMDCLTSVL
S29498          CFGKGSHFLA DVLWQINKTV VGNFGEARIQ EEEGRNESSS NDMDCLTSVL
BAA82405        CFGKGTQFLA AVLWQLNGTK ITDFGEPRIQ QEEGQNQSFS NGLACLDMVL
BAA02233        CFGKGTQFLA AVLWQLNGTK ITDFGEPRIQ QEEGQNQSFS NGLACLDMVL
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        VFNLCLQYFQ HHQWP..... .......... .......... ..........

P14719          RITGVTEKDL SLEYDCLALN LHGMIRHTIR LRRKQPSKEC PSHIA.....
S29498          RITGVTEKDL SLEYDCLALN LHGMIRHTIR LRRKQPIDHR SIYYIVAGCS
BAA82405        RIADVKEEDL LLQYDCLALN LHGLRRHTVR LSRKNPIDHH SIYCIIAVCS
BAA02233        RIADVKEEDL LLQYDCLALN LHGLRRHTVR LSRKNPSKEC F.........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........
```

FIG. 11

```
P14719          .......... .......... .......... .......... ..........
S29498          LLLMFINVLV IVLKVFWIEV ALFWRDIVTP YKTRNDGKLY DAYIIYPRVF
BAA82405        VFLMLINVLV IILKMFWIEA TLLWRDIAKP YKTRNDGKLY DAYVVYPRNY
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

P14719          .......... .......... .......... .......... ..........
S29498          RGSAAGTHSV EYFVHHTLPD VLENKCGYKL CIYGRDLLPG QDAATVVESS
BAA82405        KSSTDGASRV EHFVHQILPD VLENKCGYTL CIYGRDMLPG EDVVTAVETN
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

P14719          .......... .......... .......... .......... ..........
S29498          IQNSRRQVFV LAPHMMHSKE FAYEQEIALH SALIQNNSKV ILIEMEPLGE
BAA82405        IRKSRRHIFI LTPQITHNKE FAYEQEVALH CALIQNDAKV ILIEMEALSE
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

P14719          .......... .......... .......... .......... ..........
S29498          ASRLQVGDLQ DSLQHLVKIQ GTIKWREDHV ADKQSLSSKF WKHVRYQMPV
BAA82405        LDMLQAEALQ DSLQHLMKVQ GTIKWREDHI ANKRSLNSKF WKHVRYQMPV
BAA02233        .......... .......... .......... .......... ..........
Athdc120c9      .......... .......... .......... .......... ..........
BAA85894        .......... .......... .......... .......... ..........

P14719          .......... .......... .....
S29498          PERASKTASV AAPLSGKACL DLKHF
BAA82405        PSKIPRKASS LTPLAAQKQ. .....
BAA02233        .......... .......... .....
Athdc120c9      .......... .......... .....
BAA85894        .......... .......... .....
```

FIG. 11 CONT'D.

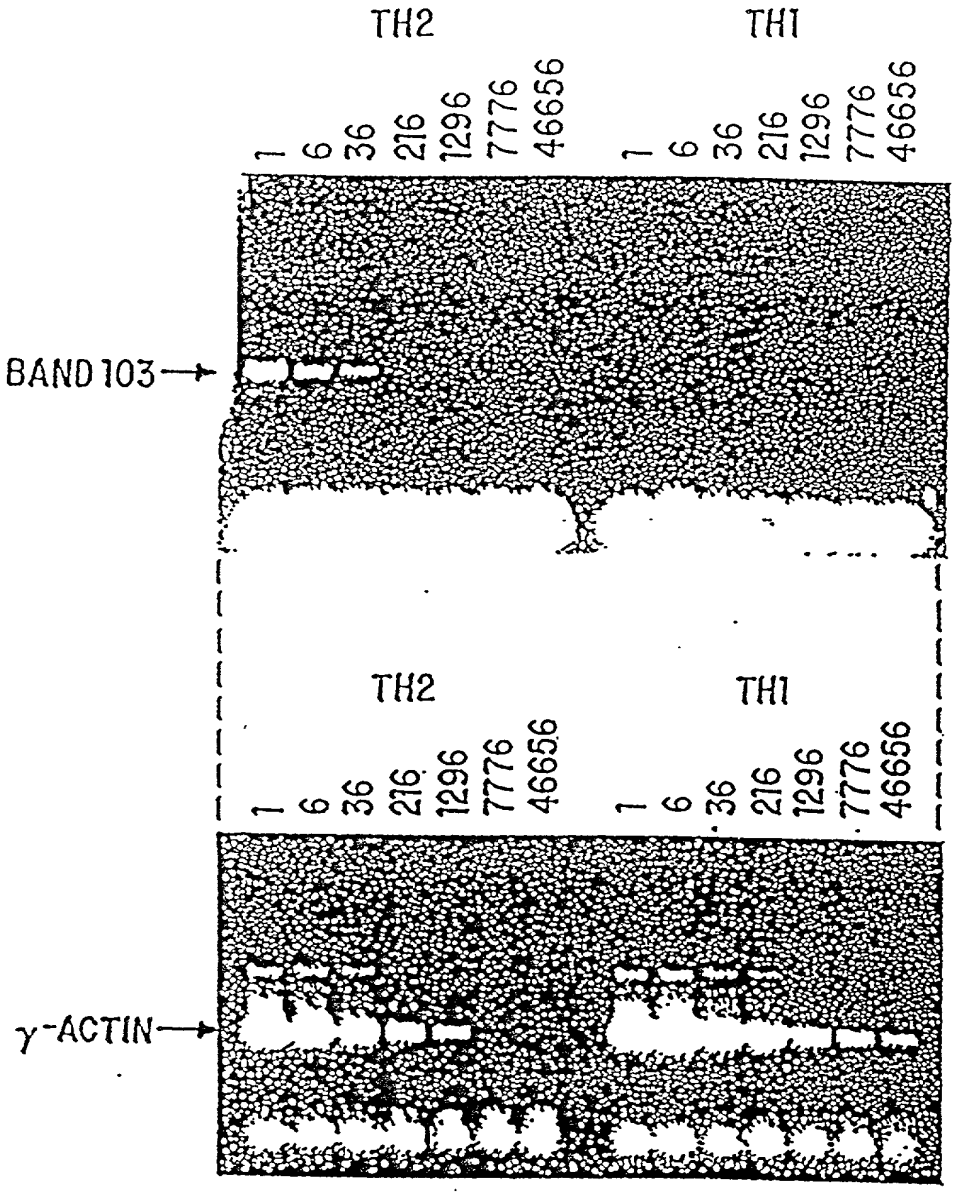

FIG. 12

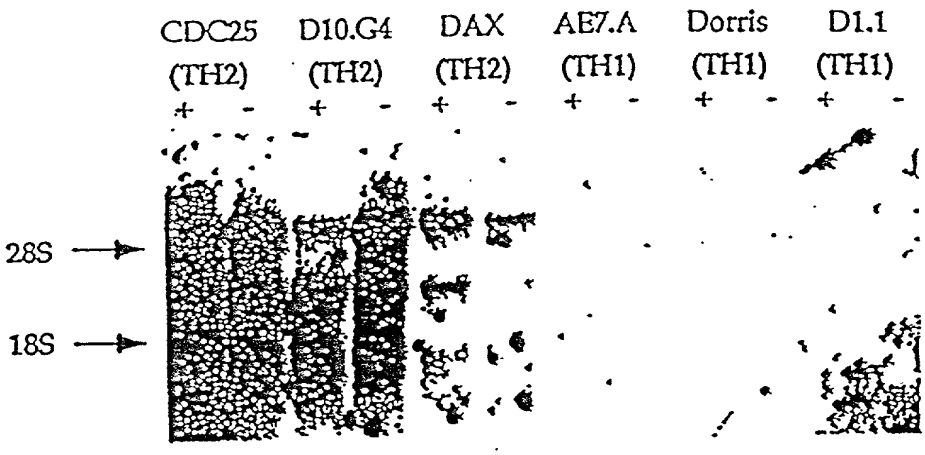
CDC25
(TH2)
D10.G4
(TH2)
DAX
(TH2)
AE7.A
(TH1)
Dorris
(TH1)
D1.1
(TH1)
+ - + - + - + - + - + -
28S
18S

FIG. 13

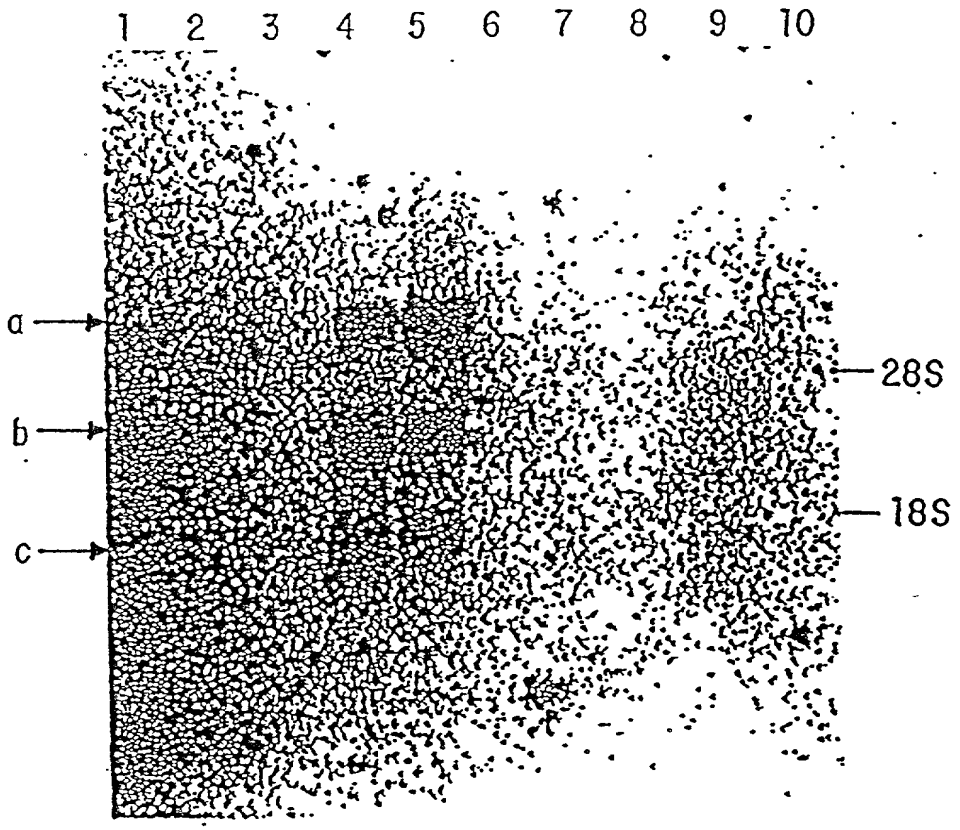

FIG. 14

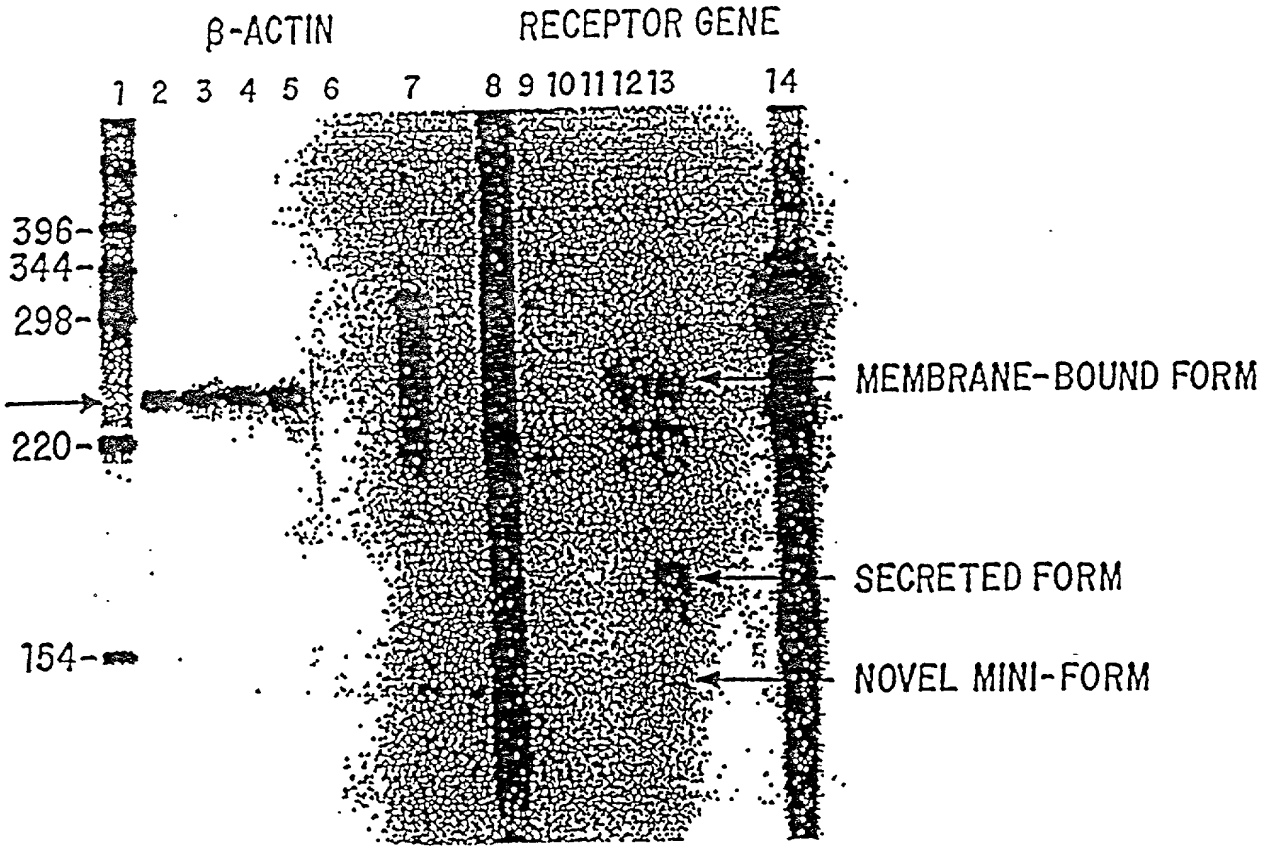
β-ACTIN
RECEPTOR GENE
1 2 3 4 5 6 7 8 9 10 11 12 13 14
396-
344-
298-
220-
154-
MEMBRANE-BOUND FORM
SECRETED FORM
NOVEL MINI-FORM

FIG. 15

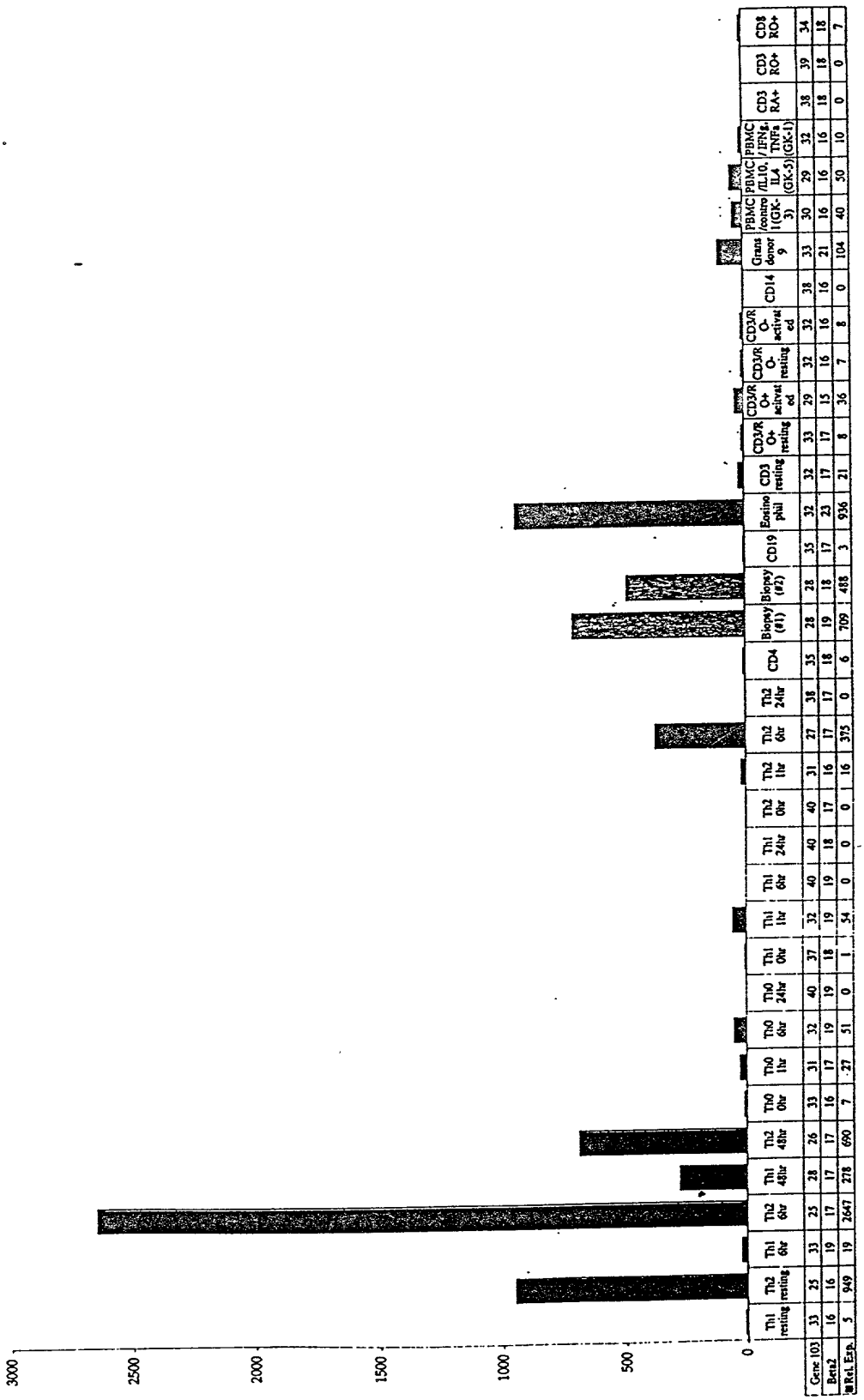
Relative Expression (CD14 #8 (CC007) resting used as reference sample)
3000
2500
2000
1500
1000
500
0
Gene 103
Beta2
Rel. Exp.
Th1 resting
Th2 resting
Th1 6hr
Th2 6hr
Th1 48hr
Th2 48hr
Th0 0hr
Th0 1hr
Th0 6hr
Th0 24hr
Th1 0hr
Th1 1hr
Th1 6hr
Th1 24hr
Th2 0hr
Th2 1hr
Th2 6hr
Th2 24hr
CD4
Biopsy (#1)
Biopsy (#2)
CD19
Eosino phil
CD3 resting
CD3/R O+ resting
CD3/R O+ activated
CD3/R O- resting
CD3/R O- activated
CD14
Grass donor 9
PBMC /contro l (GK-3)
PBMC /IL10, IL4 (GK-5)
PBMC /IFNg, TNFa (GK-1)
CD3 RA+
CD3 RO+
CD8 RO+

FIG. 16

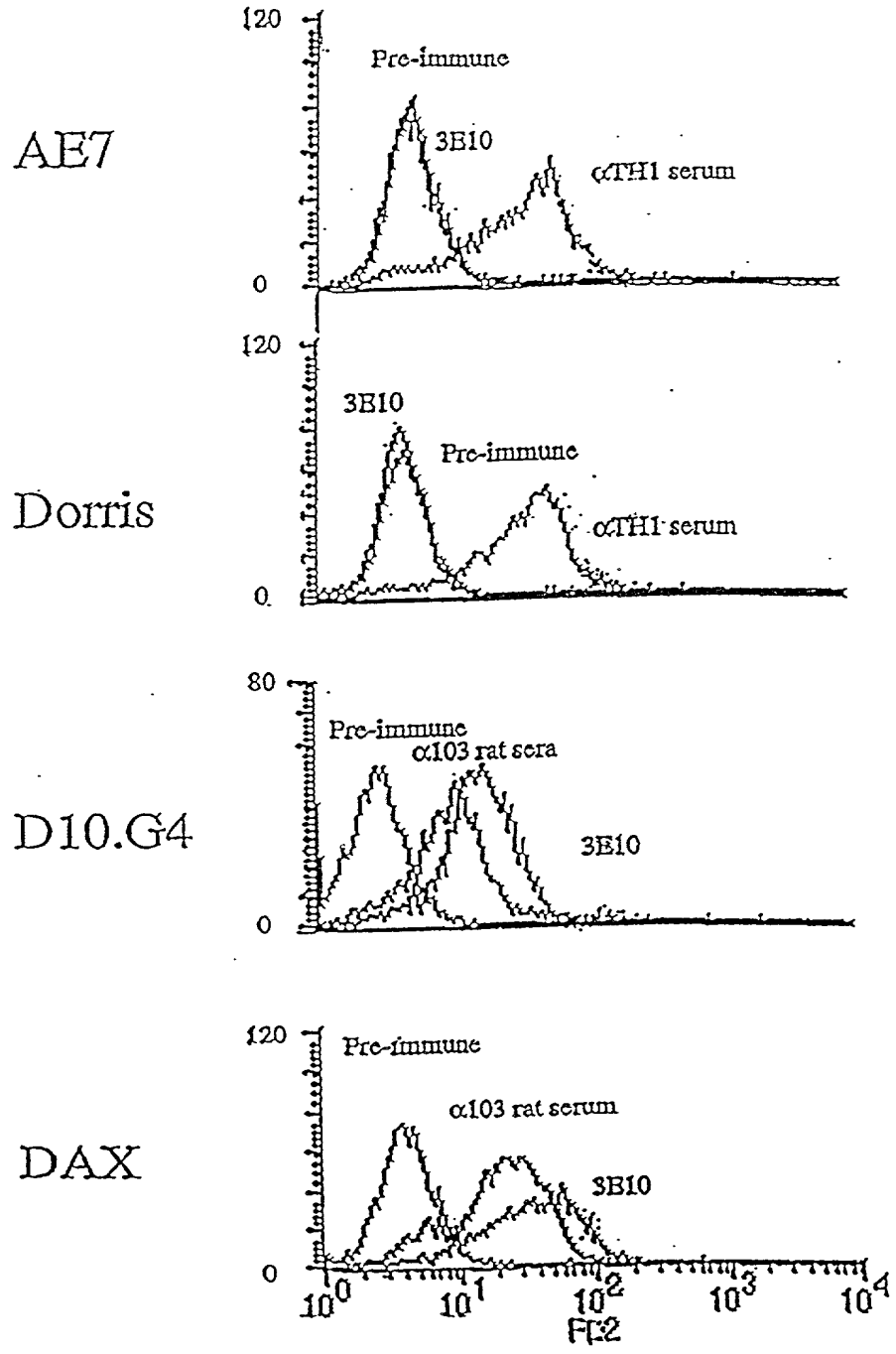
AE7
120
Pre-immune
3B10
αTH1 serum
0
Dorris
120
3B10
Pre-immune
αTH1 serum
0
D10.G4
80
Pre-immune
α103 rat sera
3B10
0
DAX
120
Pre-immune
α103 rat serum
3B10
0
10^0
10^1
10^2
10^3
10^4
FL2

FIG. 17

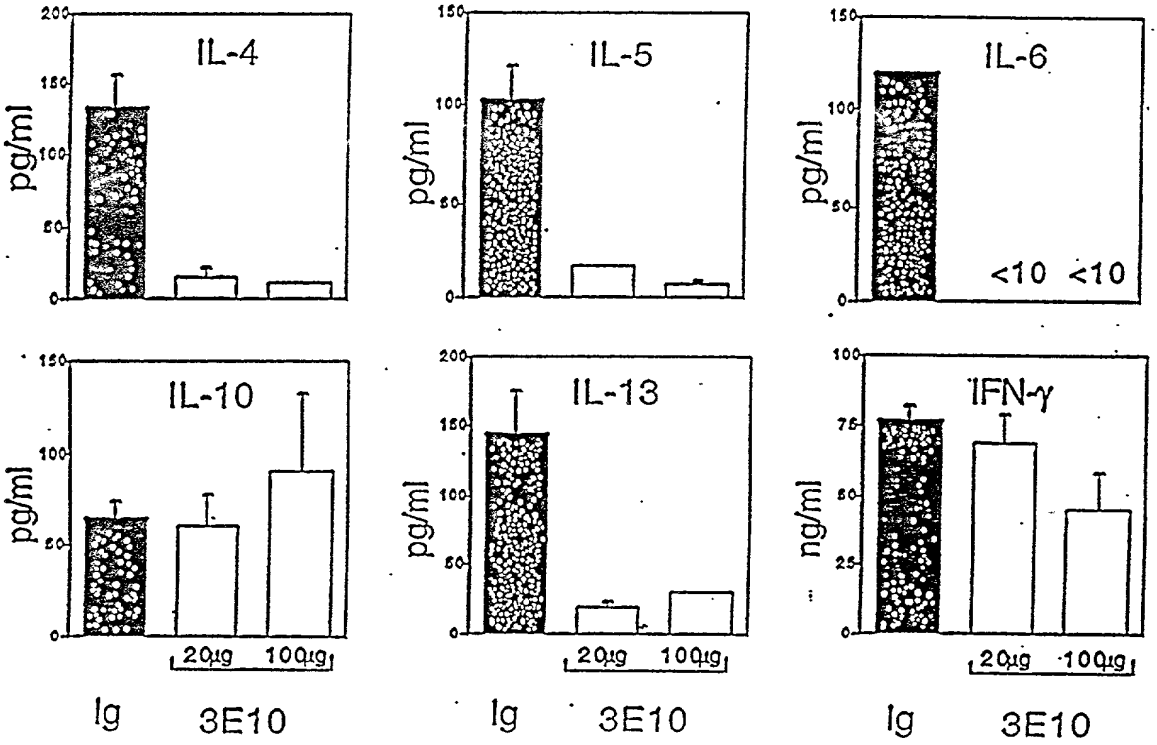
IL-4
pg/ml
IL-5
pg/ml
IL-6
pg/ml
<10 <10
IL-10
pg/ml
IL-13
pg/ml
IFN-γ
ng/ml
20µg 100µg
Ig 3E10
20µg 100µg
Ig 3E10
20µg 100µg
Ig 3E10

FIG. 18

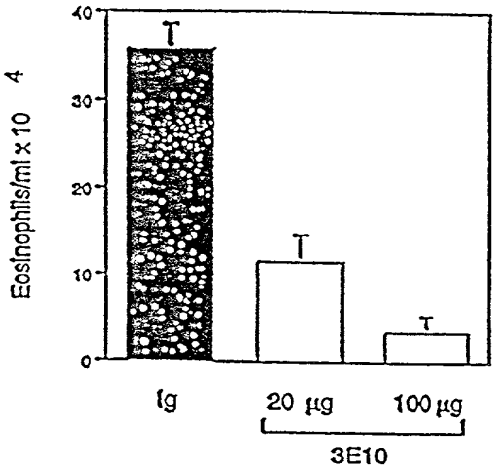

FIG. 19A

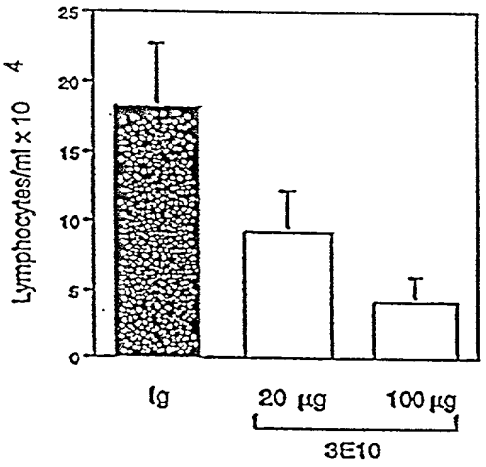

FIG. 19B

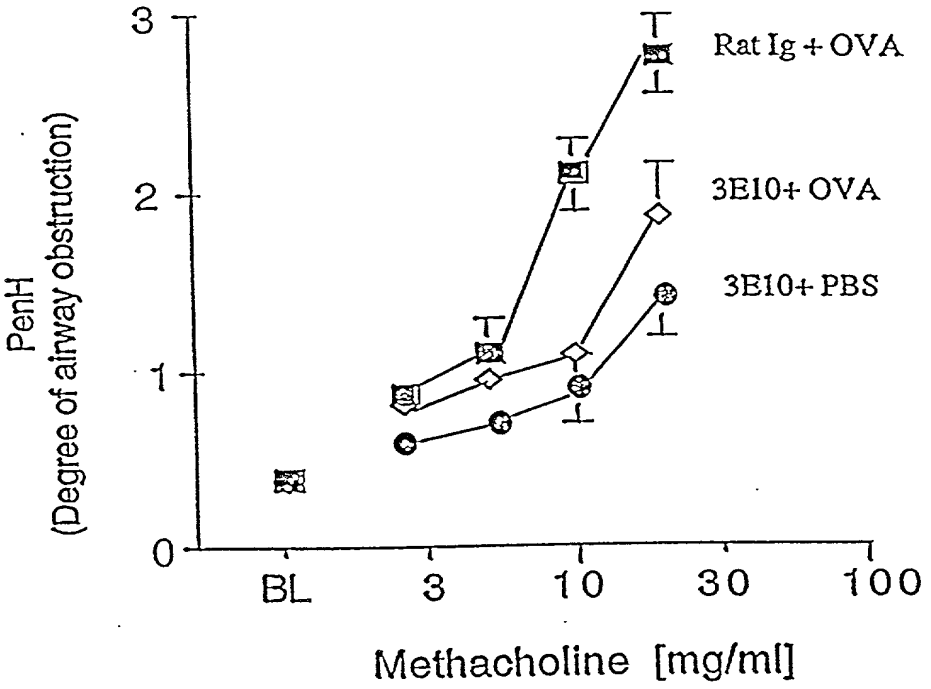
3
2
1
0
PenH
(Degree of airway obstruction)
BL
3
10
30
100
Methacholine [mg/ml]
Rat Ig + OVA
3E10+ OVA
3E10+ PBS

FIG. 20

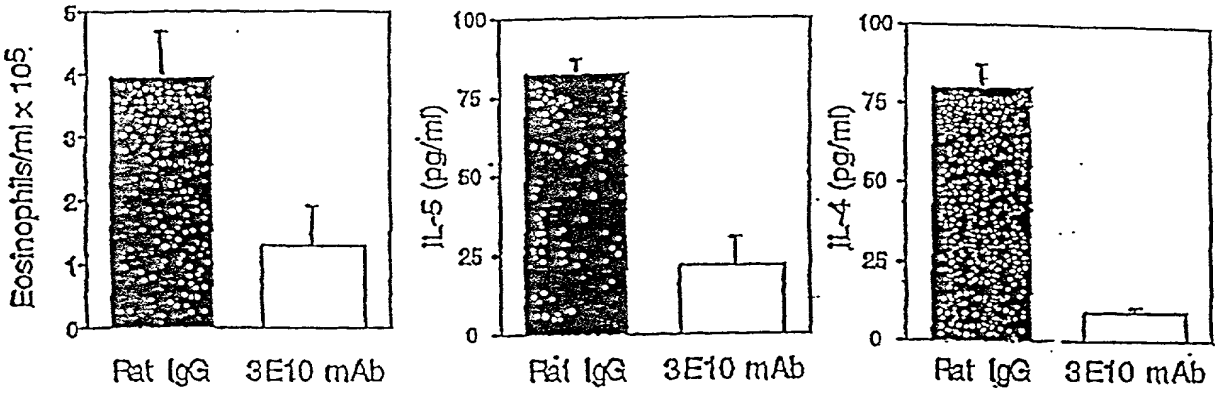
Eosinophils/ml x 10⁵
0
1
2
3
4
5
Rat IgG
3E10 mAb
IL-5 (pg/ml)
0
25
50
75
100
Rat IgG
3E10 mAb
IL-4 (pg/ml)
0
25
50
75
100
Rat IgG
3E10 mAb

FIG. 21A

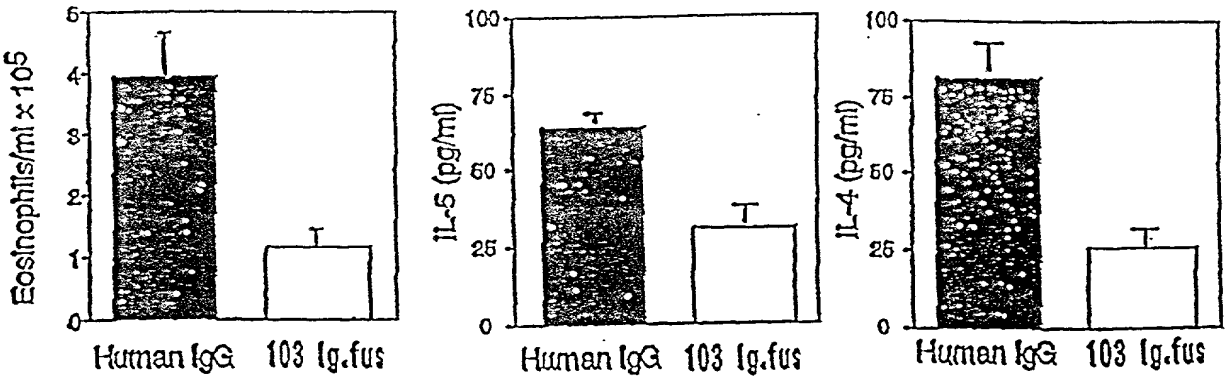
Eosinophils/ml x 10⁵
0
1
2
3
4
5
Human IgG
103 Ig.fus
IL-5 (pg/ml)
0
25
50
75
100
Human IgG
103 Ig.fus
IL-4 (pg/ml)
0
25
50
75
100
Human IgG
103 Ig.fus

FIG. 21B

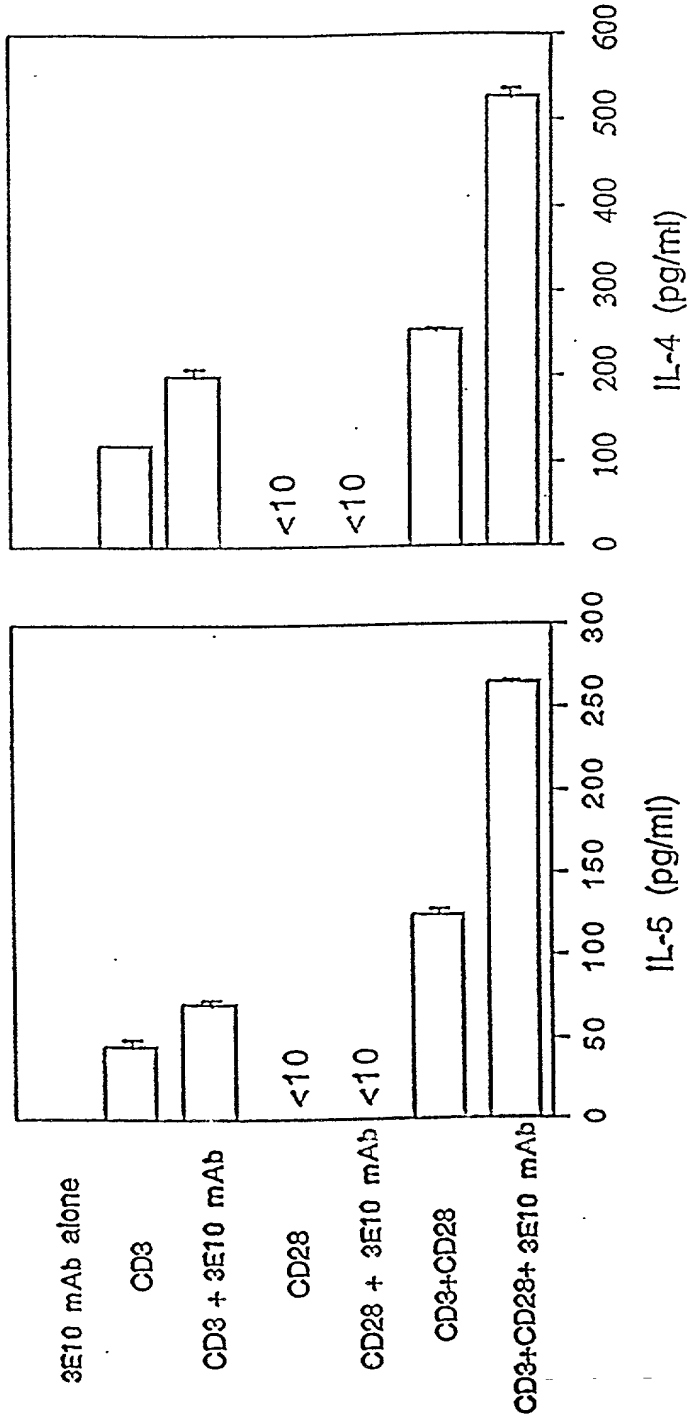
IL-4 (pg/ml)
0
100
200
300
400
500
600
<10
<10
IL-5 (pg/ml)
0
50
100
150
200
250
300
<10
<10
3E10 mAb alone
CD3
CD3 + 3E10 mAb
CD28
CD28 + 3E10 mAb
CD3+CD28
CD3+CD28+ 3E10 mAb

FIG. 22

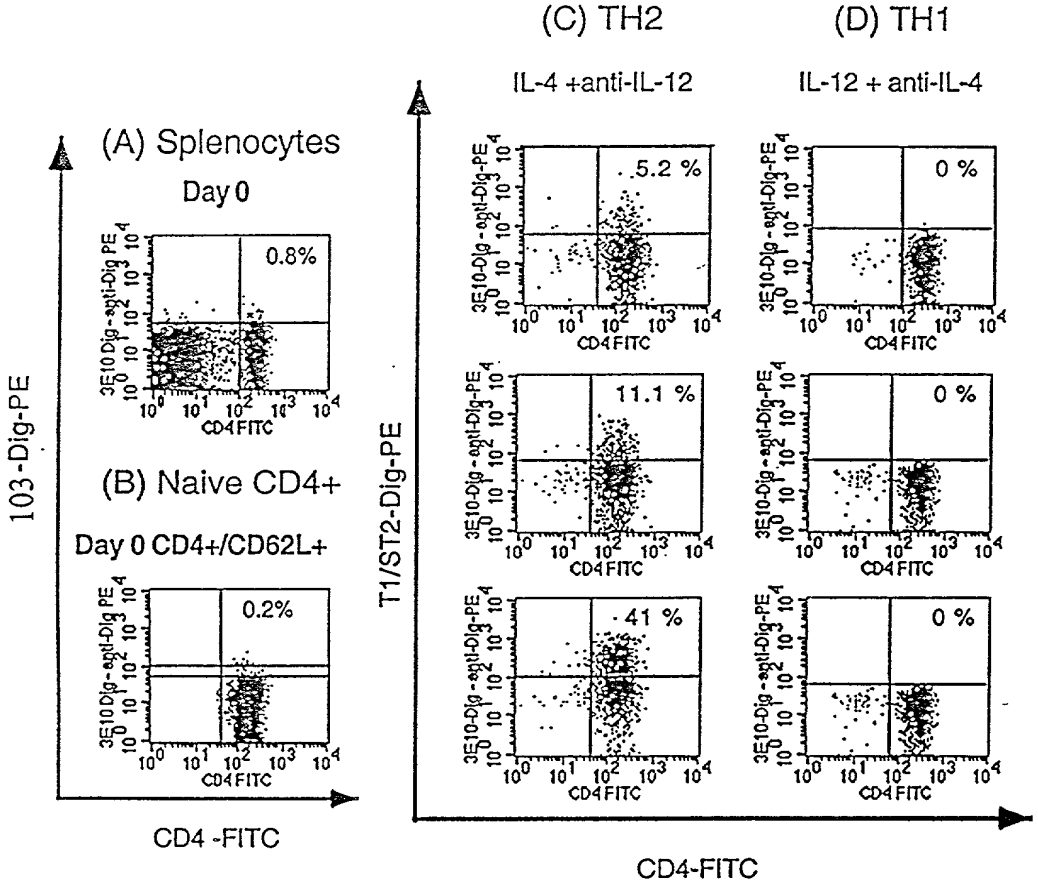
(A) Splenocytes
Day 0
0.8%
(B) Naive CD4+
Day 0 CD4+/CD62L+
0.2%
103-Dig-PE
CD4 -FITC
(C) TH2
IL-4 +anti-IL-12
5.2 %
11.1 %
41 %
(D) TH1
IL-12 + anti-IL-4
0 %
0 %
0 %
T1/ST2-Dig-PE
CD4-FITC
3E10 Dig - anti-Dig PE
CD4 FITC

FIG. 23

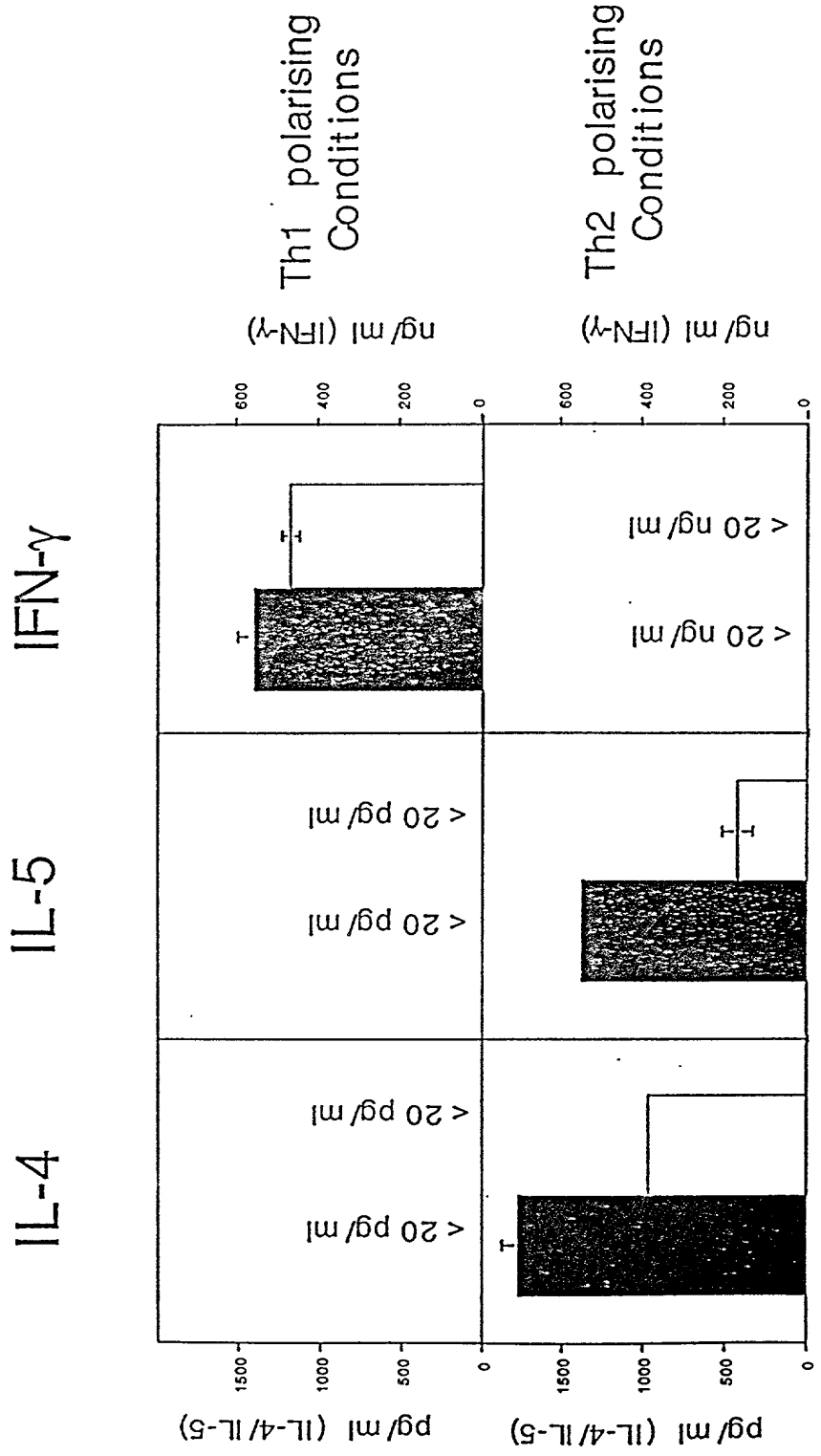
Th1 polarising Conditions
Th2 polarising Conditions
ng/ml (IFN-γ)
ng/ml (IFN-γ)
IFN-γ
IL-5
IL-4
< 20 ng/ml
< 20 ng/ml
< 20 pg/ml
< 20 pg/ml
< 20 pg/ml
< 20 pg/ml
Ig 103
Ig 103
Ig 103
pg/ml (IL-4/IL-5)
pg/ml (IL-4/IL-5)
0
200
400
600
0
500
1000
1500

FIG. 24

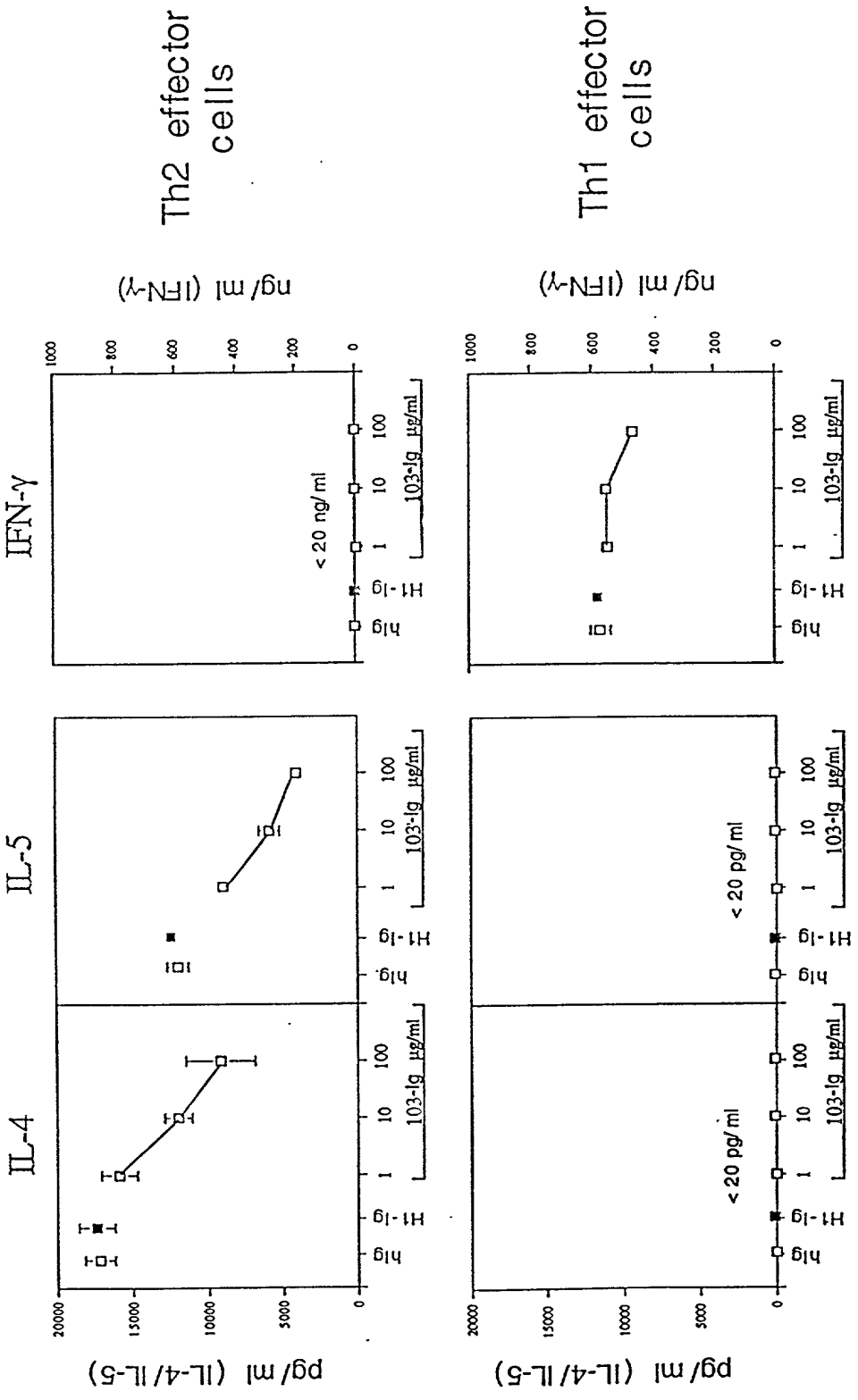
Th2 effector cells
Th1 effector cells
IL-4
IL-5
IFN-γ
pg/ml (IL-4/IL-5)
ng/ml (IFN-γ)
< 20 pg/ml
< 20 ng/ml
hlg
H1-lg
103-lg µg/ml

FIG. 25

(a) Eosinophils
Eosinophils/ml x 10⁴
25
20
15
10
5
0
Untreated
Rat Ig
103 mAb
(b) IL-5
IL-5 (pg/ml)
500
400
300
200
100
0
Untreated
Rat Ig
103 mAb
(c) IgE
OVA specific IgE (U/ml)
6000
5000
4000
3000
2000
1000
0
Ig
103 mAB

FIG. 26